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WORKSHOP ON HUMAN GENE MAPPING

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J. BENNETT JOHNSTON and JAMES A. McCLURE are Ex Officio Members of the Subcommittee

MEMORANDUM OF THE CHAIRMAN

To: Members of the Senate Committee on Energy and Natural Resources:

The Department of Energy's (DOE) national laboratories represent a significant Federal research and development expenditure and a powerful scientific resource. These laboratories have excellent scientific and engineering experts on staff and on loan from industry and academia.

One important Federal R&D concern is the "human genome" initiative. The human genome is the set of genetic instructions guiding the development and functioning of cells of the human body. The genome determines which cells form each organ, and the genome of an individual also determines the likelihood of developing known genetic diseases and the relative propensity to develop other more common diseases. Thus, an ability to read the instructions encoded in the genome is thought to have the potential to facilitate the identification of individuals at risk in a given environment and to stimulate the development of new methods for treating diseases.

Mapping the human genome is the process of locating specific regions of given chromosomes to establish the locations of genes known to serve particular functions. Sequencing the human genome would take this process a step further, to specify the precise physical location of each of the bases.

Federal research on the human genome is now concentrated primarily in two agencies—the Department of Energy and the National Institute of Health. DOE's research in this area is coordinated by its Office of Health and Environmental Research (OHER) and DOE-supported work is carried out at Lawrence Livermore National Laboratory, Los Alamos National Laboratory, and Columbia University.

DOE's role in human genome research is an outgrowth of the mission of OHER to understand the health effects of radiation and other byproducts of energy production. The OHER mission in human genetics has led to the initiation and support of a number of research and technological developments that are closely linked to the human genome mapping and sequencing project.

In July 1987 Senator Domenici, Ranking Minority Member of the Subcommittee on Energy Research and Development, introduced S. 1480, the Department of Energy National Laboratory Cooperative Research Initiatives Act. This legislation would change the research environment in the DOE National Laboratories in a way that will promote more involvement with universities and private firms. A portion of that bill deals with research on the mapping of the human genome.

It is because of this legislation and the current interest in the human genome project that Senator Domenici requested a workshop to discuss some the issues surrounding the human genome. This workshop provided the Subcommittee with an excellent overview of the genome initiative.

J. BENNETT JOHNSTON, *Chairman.*

A G E N D A

Workshop on Human Gene Mapping

August 31, 1987
1:00 p.m. to 4:00 p.m.
Santa Fe, New Mexico

1:00	OPENING STATEMENT and Introduction of Workshop Participants	Senator Pete V. Domenici United States Senator
1:15-2:30	DISCUSSION	Panel
2:30-2:45	BREAK	
2:45-3:45	CONTINUED DISCUSSION	Panel
3:45-4:00	CLOSING REMARKS	Senator Domenici

Possible Issues of Discussion

- What are the benefits of mapping the human genome? And what are the additional benefits of sequencing the genome?
- What have the National Laboratories done to date on mapping the human genome?
- What role should the National Laboratories play in the future?
- How should the DOE, NIH and the NSF coordinate their efforts on mapping the genome?
- How should business be involved in the project? What special technology management issues need to be addressed?

LIST OF INVITEES

DEPARTMENT OF ENERGY
Dr. Charles Delisi

NATIONAL INSTITUTE OF HEALTH
Dr. Ruth Kirschstein

NATIONAL SCIENCE FOUNDATION
Dr. David Kingsbury

LOS ALAMOS NATIONAL LABORATORY
Dr. George Bell

LAWRENCE LIVERMORE NATIONAL LABORATORY
Dr. Anthony V. Carrano

Lawrence Berkeley Laboratory
Dr. Paul Silverman

OFFICE OF TECHNOLOGY ASSESSMENT
Dr. Robert Cook-Deegan

COLLABORATIVE RESEARCH
Dr. Thomas Oesterling

LARGE SCALE BIOTECHNOLOGY, INC.
Dr. Norman Anderson

CONTENTS

	Page
Memorandum of the Chairman	III
Agenda	V
List of invitees	VII
Workshop discussion	1

WORKSHOP ON HUMAN GENE MAPPING

MONDAY, AUGUST 31, 1987

SANTA FE, NM.

Senator DOMENICI. This isn't an official or formal committee hearing, but the Energy Committee and the United States Senate, principally because of the relationship of the Department of Energy's laboratories, is going to have some formal hearings on this subject in the not too distant future, and it seemed to me that in preparation for hearings that it would be, number one, good to invite our wonderful visitors who have come from around the country, to have a chance to visit Santa Fe and we thought that wouldn't be too big an imposition. [Laughter.]

And then we thought it would be nice to sort of have a seminar kind of atmosphere to talk about, both for my benefit and the staff, majority and minority staff of the committee's benefit on this subject of mapping and sequencing of the human genome.

Now, for the members of the press, if they will bear with us for at least part of this discussion, I'm sure they will get a better feel for what this subject, mapping of the genome and the sequencing of it is.

But essentially, before I have everyone introduce themselves and then proceed to discuss with you briefly what I thought the goals should be, let me just suggest to you that this matter, in my opinion, at least, is a serious and significant part of the national discussion that has been taking place recently under the rubric of competitiveness.

Now, I know that frequently a subject as significant as this, in terms of wellness and health and diagnostic potential, and everything that goes with that, biochemical research, the pharmaceutical industry, health delivery, the delivery of health care in the future, those are all much more frequently thought of as much more in-depth words than this word competitiveness.

But frankly, the United States Congress recently, in adopting a so-called trade bill, was engaged in a serious discussion of America's potential competitiveness in the newly integrated world market, and we were constantly talking about, let's make sure we are doing what we should to remain competitive.

And because I'm privileged, for you outsiders that are not from New Mexico, because I'm privileged to have both Los Alamos and Sandia, White Sands Missile Range, the Air Force Special Weapons Lab, in my state, along with some universities, I am frequently the beneficiary of a marvelous education in science.

And so it came to me very quickly during that debate on so-called trade and competitiveness that an issue such as the mapping and sequencing of the human genome, as I indicated, while terribly important in terms of our understanding diseases and being able to

cure them, that it also was becoming a very, very significant competitive situation, vis-a-vis at least the Japanese, but not limited to them.

We are led to believe, and some of you during the day may be able to shed more light on it, that the Japanese have made a commitment, I think Dr. Delisi and others have first-hand information from some of their people, that they had just decided that one of the most exciting biochemical issues around is the technology of mapping and sequencing the human genome, or human genes, and that they have set some goals to get on with doing it in a national way.

I don't want anyone to think that the United States of America isn't doing a lot. You'll find out that we're doing a lot. But we're not doing it under a goal-oriented plan saying, we're going to get it all done within a certain period of time, and we have not committed to that kind of goal, nor the resources, and thirdly, we have not yet put together the collaborative mechanism, for lack of a better word, between the various parts of the United States Government that play a vital role.

We all know that the National Institutes of Health, we'll hear from them today, in fact, we have a letter here from the director, which I'll read shortly, National Science Foundation, the Department of Energy, and obviously many of our universities, are involved in one way or another in this issue of the human genome, but we have not made a decision as a nation as to how that should be coordinated and how much we ought to be spending each year and what our national goal, if any, should be.

I'm led to believe, and I hope the experts here will correct this if I'm wrong, that if we proceed along the lines that we're not involved in a noncollaborative way and without an overall goal of mapping and sequencing the entire genome, that we conceivably could get there in thirty to fifty years.

Some have said you won't even get there that quickly if you continue down the course you're on. And that if, conversely, if we were in a collaborative manner with sufficient resources and use of the resources that we've got, it would not be an unreasonable thing to suggest that the United States ought to get there in five to ten years.

I am also informed that we have a mild window of opportunity in that while the Japanese have been in many areas feeding us with our own knowledge base and getting there quicker than us in terms of application or enabling technology, that they are slightly behind the power curve here because of equipment, that perhaps they are retooling in terms of their computer systems and the like.

But if they continue with a very high-powered scientist that has the appropriate ear of the government, and I understand there is such a person, if he succeeds in getting the resources, then obviously, unless the United States decides to move ahead, they will probably get there first and have what I consider now, and you all can certainly help me with more finesse and science, but basically if they get there first, what they own is an ability to transfer huge amounts of knowledge to their scientific community from which rather dramatic improvements can be made in terms of their industries that are involved, be it in the pharmaceutical industry,

the broad health care industry, and just succeeding in coming up with cures and methods of curing diseases both hereditary and otherwise.

So it seems to me that it does properly come under the rubric of competitiveness, but in another sense, we have set some big goals for ourselves in other areas. We wanted to get to the moon once and we said we would. We've set some very significant goals in some of our military procurement and development. We've set some other goals in the scientific areas.

And frankly, I am personally, as one senator, just from what I know now, and you all may either discourage that current state of mind or encourage it, I am convinced that we could probably have no better goal than to get this done, and no more significant goal, from the standpoint of wellness and disease control and the delivery of health care in the decades to come, than to go ahead and commit to the mapping and sequencing of the human genome.

Why are we doing this in New Mexico for the New Mexico press that's here? Obviously, I indicated that there were different departments of the Federal Government involved. That's true. And it just happens that the Department of Energy and at least two, maybe three, of its laboratories, for one reason or another, is involved either with computer technology or because there's an accumulation of biochemical experts and biologists in the labs that they have a role to play.

It's my understanding that it could be rather significant and as part of a collaborative effort that they would be a significant player along with NIH and others in putting together a national approach.

I introduced a bill as part of the trade bill. It did not get through because what I have just told you, obviously, in these few words of a layman, is made very complicated when you get into the jurisdiction of the committees and when you find out that there are different versions of who ought to play the lead role and how you ought to put a policy group together; should it be statutory, should it be executive only, who should chair it, who should be on it, and how should the goals be set for the mapping of the human genome.

That was too tough to get done without formal hearings, but it did stir up enough enthusiasm where I think we were close enough, if that trade bill which languished on the floor for what, three weeks, if it would have languished another three, we might clearly have gotten the players together and passed an authorization bill that set the national objective and set in place a policy group with some kind of revolving chairmanship to get on with it.

A little more difficulty in that legislation came when we started talking about the private sector involvement at this early a point, and we will have some people here discuss that today. That was harder for us to put our ideas together on, but clearly in these United States, ultimately you don't want to go through this kind of effort without taking full cognizance of the private sector of the United States, which, in the area of health delivery and breakthroughs in medical technology, has heretofore led the world.

I'm suggesting that using the word heretofore, that that might be short-lived if somebody beats us to this particular goal of the mapping and sequencing of the human genome.

I will close, after reading Dr. Wyngaarder's letter, by suggesting that it's clear to me that the United States of America has plenty, at least for now, basic knowledge. We may in the next few decades, if we aren't careful, be short in that area, but we are making the knowledge breakthroughs.

The problem is that some other countries in the world are catching up there, but in the meantime they're applying knowledge a little more proficiently and a little more efficiently than we are, and if we don't find a way around that problem, it's going to be pretty tough for the next two or three decades to be competitive.

In addition to people from the Department of Energy and National Science Foundation and others, I wanted to quickly indicate that obviously one of the premiere research agencies in the world when it comes to health care and the research, biochemical research and biology, our National Institutes of Health are second to none.

And I have a letter saying that—I'll just read it. It's brief:

I'm sorry I cannot attend the workshop on the human genome mapping on August 31 in Santa Fe. Dr. Ruth Kirschstein, the director of the National Institutes of General Medical Sciences, will represent the National Institutes of Health as the preeminent biomedical research institution in the United States.

The NIH, of course, has a major role in the task of characterizing human genetic material, genetic diseases, and will continue such a role in the efforts to map and sequence the human genome.

I know that you, as a member of the Senate Appropriations Committee, Subcommittee on Labor, Health and Human Services, and related agencies, are well aware of the central position the NIH has in this field.

I understand that your staff has tentatively accepted my invitation for you to visit the NIH on September 8th. We will be pleased at that time to provide an assessment of the research being conducted in our intramural facilities and the activities being supported by NIH in universities and research laboratories throughout the country, including those activities being supported in New Mexico.

In the meantime, in the interim, Dr. Kirschstein will be pleased to provide you with information, not only about projects related to the human genome but all other activities at the Institute.

I look forward to your visit.

Sincerely,

Dr. JAMES B. WYNGAARDER, *Director.*

With that, let me start on this side, and would each person introduce themselves, and then I will ask for some quick comments, and I'll tell you what my thoughts were for the afternoon.

Dr. KIRSCHSTEIN. I'm Dr. Ruth Kirschstein. I'm the director of the National Institute of General Medical Sciences, National Institutes of Health.

Dr. KINGSBURY. David Kingsbury, the assistant director for biological, behavioral and social sciences, the National Science Foundation.

Dr. DELISI. Charles Delisi, Department of Energy.

Mr. OESTERLING. Thomas Oesterling, I'm the president of Collaborative Research, Inc., located in Bedford, Mass.

Dr. CARRANO. I'm Tony Carrano, program leader for genetics at Lawrence Livermore National Laboratory. I'm also the principal investigator of the human genome project at that laboratory.

Dr. BELL. I'm George Bell, leader of the theoretical division at the Los Alamos National Laboratory.

Dr. COOK-DEEGAN. I'm Bob Cook-Deegan from the Office of Technology Assessment, which is a small analytical agency for the U.S.

Congress. I'm here because we've been engaged in a project looking at federal policy in mapping and sequencing since last December.

Dr. SILVERMAN. I'm Paul Silverman, associate director of the Lawrence Berkeley Laboratory and head of the biology and medicine division, in which division we have recently established a center for human genome.

Mr. ANDERSON. I'm Norman Anderson with Large Scale Biotechnology, Incorporated, in Rockville, Maryland.

Senator DOMENICI. Well, let me say thanks again to all of you. Would anybody, anyone care, based upon my rambling on, to add anything to what I've said, or clearly, if I've said something that's not too right, correct it? Anyone want to make any observations or comments?

[No response.]

Senator DOMENICI. Well, let us move along, and let me tell you what I'd like to do. The purpose, as I see it, is to begin to build a legislative record. The goals of this workshop, as I see them, are to define, if we can, the benefits of mapping and sequencing the human genome, discuss some possible ways to accomplish these tasks, and discuss the different roles of NIH, NSF and the Department of Energy, and discuss the role of the National Labs through DOE and discuss how the private sector might best be involved.

If we can proceed on that basis, why don't I start with the first one, the benefits of mapping and sequencing, and ask Dr. Charles Delisi of DOE, and you, Ruth, and Dr. Kingsbury, if you could just begin and perhaps in the order that I've called your names off, to discuss that very first and fundamental issue, the benefits of mapping.

Dr. DELISI. Mapping, and I expect maybe some people who are totally aware of the definitions of these things, roughly we can think of mapping as trying to identify on which chromosome a particular gene or DNA fragment might be and where on the chromosome it might be.

It's not very precise information. For example, right now many disease genes have been mapped to within a million bases, so somewhere in the region of a million bases of DNA might lie the gene for cystic fibrosis, for example. It happens to be on Chromosome 6.

But there are forty or fifty other genes in that region. So we want to develop more precise methods for locating the position of genes. And then, once the position has been located, to try to understand the internal structure of genes, and that's what sequencing is about.

And with sequencing, you can then—we can be able, we will be able to tell what's different between one person's gene and another person's, why is it that one person is susceptible to a particular disease and another person is less susceptible.

So in order to answer those questions precisely, we go to sequencing or to more precise methods for developing information about the internal structure of genes.

The Department of Energy, of course, has a major interest in this, in part because we need to understand variability in the human population, variability to disease susceptibility, variability in resistance, and in part, as Senator Domenici indicated, the De-

partment, the National Laboratories have unique capabilities to address these questions.

I might add that this project is, although it has a substantial biological component, what makes it a little bit unusual is that it is not just a biological project. That is to say it requires computer analysis, it requires engineering.

We heard a little bit—Senator Domenici referred to the Japanese efforts. There are two things going on in Japan right now. One, they're developing a robot. Archie Wada, who is an old colleague of mine, is behind that project.

The second thing is they've just published a map, a clone map of E. coli, so they're moving very, very rapidly in this area.

What we heard this morning at Los Alamos was something very exciting. Although we're not developing a robot, we have very, very innovative technologies under development, technologies which would make sequencing the whole genome possible, if they're successful, in a month, if they were successful, and it would happen at about a tenth of a cent per base. At current cost, it's like a dollar a base.

So the country, the nation has to pay the bill for these, I think, to make major, certainly to make major advances here and of course, again, as we heard, this is something, this is not just a National Laboratory project, it's not just the Department of Energy.

I've been emphasizing for a year, since I started talking about this, I think every federal agency in Washington should have a major interest in this, and certainly NIH is the premiere institute, institutes in the world, a premiere organization in biomedical research was basically founded in the field of molecular genetics, and I think this is something we can all work together on very, very effectively.

Senator DOMENICI. Thank you very much.

Dr. KIRSCHSTEIN. I agree with Dr. Delisi, and we believe firmly that the collaborative nature of this kind of a project is absolutely essential.

Scientists have been working in this field for over thirty years now. The biologic revolution that everybody knows a great deal about started about thirty-five years ago now, when Watson and Crick discovered the way in which DNA is put together, the so-called double helix.

From there, there has been an enormous expansion, and discovery has followed discovery. Right now there's a concerted effort to pinpoint the specific locations of genes on chromosomes for particular inherited diseases.

Researchers have already mapped the genes approximately, not specifically, but approximately for Huntington's disease, Duchene's muscular dystrophy, retinal blastoma, which is a cancer of the eye in children, some forms of manic/depressive disease, cystic fibrosis, as Dr. Delisi mentioned, and indeed, most recently, cancer of the colon.

Finding these genes approximately will allow researchers to study them and make copies of them and learn what protein each gene calls for, to understand then ways to treat these disorders and to perhaps replace defective genes. But this is going to be a major challenge to do the entire project.

I'm delighted to hear from Dr. Delisi that the technical innovations are moving so rapidly and that indeed these challenges can be met by all of us collaborating together.

Dr. Kingsbury will probably tell you approximately how we all plan to collaborate, but I can tell you about several specific things that are going on.

As the information in these areas develops, there is going to be a great deal of need for a data base to handle it. And some years ago, spurred on by Dr. Walter Goad, from Los Alamos National Laboratory, the National Institute of General Medical Sciences and NIH, set up a collaborative project at Los Alamos to set up a group called GenBank.

That is providing information to the scientific community in general at a great rate. That contract is due to be renewed momentarily, and Los Alamos National Laboratory has a premiere part in that.

Secondly, because we so much want to collaborate, a member of my staff will join on a detail Dr. Delisi's staff tomorrow morning to work for three months on this project in collaboration with the Department of Energy. That means that what we're doing will be known to Dr. Delisi. What Dr. Delisi's staff is doing and what's being done at Los Alamos and Livermore and some of the other laboratories will be known to us, and we plan to work together over and over again.

This is a project that is not just an American project, Senator. It's an international project. We have been in touch with the people at the European Molecular Biology Laboratory, Dr. Delisi has a contact in Japan, and altogether we think the world will benefit through a collaborative effort.

Senator DOMENICI. Thank you very much.

Dr. Kingsbury.

Dr. KINGSBURY. I think that the two speakers have summarized in some extent the power and excitement and the applicability of the sequencing and mapping studies. I think that the potential of understanding inherited disease, the potential of finding new pharmacologically active compounds within the human genome is an exciting possibility.

Clearly, this kind of molecular genetics is going to get us there.

I think that as we talk about this and as we focus on it, we have a tendency to think that the physical mapping of the genome and the derivation of that sequence is going to give us an enormous amount of information.

And it is going to give us an enormous amount of information, but it's going to be information that would, in my mind, be akin to the Encyclopedia Britannica without spaces and without commas and without periods. And it's going to be a little bit of gibberish, maybe even a lot of gibberish.

Perhaps it depends on whose estimates you follow, maybe only ten to twenty percent of the genome is really meaningful information. The other portions of it may be information that we fully don't understand and may not understand for quite a long time.

So the point I'm trying to make here is that the sequence alone of just determining that sequence is not enough, that there's a great deal more to the human genome project, if we can call it

that, a research related to the human genome as we've preferred to term it recently, that needs to be focused on, that just arriving at that sequence, while valuable and exciting and an enormous resource, is only the beginning of this project and it's not the end.

And we must keep that in mind, because we're talking about a long-term, very, very biological project.

Our ability to map something on the order of perhaps a hundred thousand functional genes in the human, is perhaps a century away. We simply don't have the mechanisms to have controlled breeding programs, and it seems unlikely that we ever will get to that in humans.

Whereas in other animal species we certainly have made enormous strides in understanding linkage maps, in understanding specific types of mutation.

Now, I guess what I would like to throw into this discussion, as we talk about the excitement of this project, is the discussion, is the concept of the biologist who wants to make the point that the biochemistry is nice, but that we must constantly relate this back to some biochemical, some biological questions about what those genes are, where they are, how they function.

And that's going to be a major effort in comparative biology. We're going to have to look at all of those data points that we derived from the mouse and from other higher animals and so some comparison.

So the perspective is that while this is a highly competitive and a highly charged sort of environment in which to work, it really is going to be an international effort, and that simply determining the sequence by itself is not enough to give you that great advantage, that you have to understand that sequence and how it functions. And that's going to take a major effort in comparative biology.

And so when we think about the balance of the human genome enterprise, we must keep in mind this entire balance. And I think those of us who have spent some time thinking about this coordination mechanism, and we'll come to that in one of your later questions, have thought about this extraordinary breadth of this project. It's not simply the one focus.

And so with that, I think I will——

Senator DOMENICI. Doctor, would you, just so I'll understand, clearly if you read in any background of this senator that I was a chemistry major and a math minor and taught algebra, please remember that that was a very short-lived avocation. [Laughter.]

And I have not been back to the blackboard or to one of those books, other than when forced upon me, in thirty-some years.

So let me just see if, in my totally layman's approach, if I might just ask you a question, because I think I understood what you said.

Am I correct that while this is going to be, in its total scope, a major international experience and require a major effort in comparative biology, that one might look at the mapping and the sequencing as a tool from which these comparative biologists and/or whatever other kind of scientists are required, from which they are apt to arrive at some very important conclusions about diseases without which we might not get those answers? Is that a fair——

Dr. KINGSBURY. That's right. Let me put it in the sense that understanding the structure of a gene or understanding the sequence of a compound that perhaps is physiologically active life, interferon or interlugen, having that sequence, but just having sequenced a big piece of DNA and having run across that sequence, first, one might not even recognize it without knowing for some biological reason that you were in the right region and it was there.

You have to have had some basic information to start with. To understand how to put that information together and use it is a further application of the toolbox that one derives from the sequence.

The sequence is where you start, but there's a lot of understanding that has to come with that. And I think that's the perspective we need to keep in mind, in that when we think of the competitive nature, I think that we must keep in mind that one has to imbed the human genome project in the mapping and sequencing in an enriched program of basic molecular biology, and I want to stress biology, because the sequence alone is not enough information to make that sequence usable.

We must constantly have it imbedded in the kind of exciting, basic, fundamental research that NIH, for example, supports so well.

Senator DOMENICI. Very good. I will soon be nicknamed, just so you will know, Doctor, the predictor of the newest science revolution, because I am firmly convinced that what you all are teaching me, especially, as I indicated, since I have so many scientists around me, I am firmly convinced we're going to make more breakthroughs in the next thirty years than we have in history.

And I think that is really what Americans better be worried about, because many of those are going to be applied in the marketplace. Obviously, if they have to do with keeping people well and getting them well and curing inherited diseases, it's more so an important thing.

But I get more and more convinced that this is going to become a much more scientific oriented world in all respects and I'm delighted we have the science to start with. I do get worried from time to time that our private sector doesn't use that science, and I'm not critical of them, we need new arrangements, I think, to get through this next two or three decades.

Dr. KINGSBURY. I think that if you listen to, as many of us have been out and about various meetings, talking about what we can do as government funders to help that interface, one of the things that the pharmaceutical industry is constantly bringing forward now is that they are totally dependent on the kind of work that's being supported at the NIH; that random synthetic chemistry, which has been the most powerful tool in the pharmaceutical industry for the past—since World War II, is really not the right answer anymore; that understanding what that cell is doing and how that compound interacts with the cell is in fact the future of that industry. This project fits into that.

Senator DOMENICI. Well, before we go to my next goal here of—is there a project and how should it be undertaken, why don't I, because we have a little time this afternoon, ask any of the rest of the guests here if they want to comment on just the observations

that we've made to this point, either mine or theirs, just a little general discussion.

Dr. BELL. I'd like to underline one of your conclusions, to emphatically agree that the essence of any human genome project should be considered as technology development. That is, we are in the position of being able to undertake this sort of contemplated exercise only because the state of technology in sequencing in the recombinant DNA field is what it is.

But it's clear that further improvements will be extremely cost effective in providing improved, more rapid, automatic, efficient and accurate instruments and processes for carrying out this sort of thing, both in producing the physical maps and in the DNA sequences.

And this means that each advance along the way is going to have immediate pay-off, both for basic biological research, for clinical practice, and for U. S. competitiveness. The program is no way analogous to something like an attempt to put a man on the moon or something like that, because every little step we take is going to be an immediate benefit to the field.

And as you so correctly perceive it, why, the ultimate products of the project, mainly the clones that constitute the physical map and which can be assembled in some repository, the sequences which can be accumulated in information resource and accessed by a computer, are themselves only tools for the further analysis of problems in biomedical research.

So I think that this is again an illustration that each step along the way, each set of clones we develop, each new set of sequences, is going to be immediately useful and beneficial and is not a program that has to wait until some pay-off long down the line, but every significant step along the way is going to be immediately seized upon by the biomedical research community, by people interested in improvement in agricultural crops, and so forth.

Senator DOMENICI. Well, I appreciate the differentiation that you've just made between the analogy that I used. On the other hand, people that know a lot more than I about it have used it from the standpoint of a commitment, not from the standpoint of it being only one goal, or one—excuse me, only one derivative benefit, and in that respect, my analogy is a bit short and I appreciate your commenting on it.

Anybody else?

Dr. COOK-DEEGAN. I had just a couple of things that I'd like to bring up again, that I think the points have been made but I'd like to emphasize them.

First of all, in connection with the Japanese efforts, I think one thing that should be understood about that is in one sense the threat's very real. In another sense, it's not too clear what the Japanese are committed to.

One thing that needs to be understood, I think, about the Japanese project is that it is exclusively focused on developing machines that would do DNA sequencing today. They haven't thought about the parts of the process of mapping and sequencing that would allow you to develop the things that are going to be sequenced.

That's in fact a much more difficult process that involves a whole lot more biology.

And also going on in Japan is there's a big dispute between two of—between media in their science and technology administration. The future of their sequencing effort is not endowed. I think something will go forward, but it's not clear what shape it's going to take or who's going to be running the show.

But, I mean, it is clear that they're going to be developing sequencing machines and machines to do other parts of DNA handling and things like that. It's not at all clear that they've done their spade work in some of the other areas.

The second point that I think that you've captured quite accurately is that I really think that the novelty of Charles' initiative started a couple of years ago was really to focus on tool construction and to focus on critical choke points, that is, technological barriers that need to be left over in order to enable research to be more efficient.

I think that's really the innovative thing that's novel about this, quote, human genome initiative.

One of the red herrings here, I think, is this idea of whether the complete human sequence is the terminal objective or whether it isn't, because I think to a certain extent that really depends on what technologies are developed and how cheap they are to use.

It's very clear that sequencing is an important component of mapping. It's very clear that a lot of people right now are doing an awful lot of sequencing, and that if it were cheaper and faster, they would do even more of it.

So it's very clear that developing that technology is crucial. I think it still is an open question of whether you want to sequence everything in the human genome. I think that will only be answered by whether it becomes cheap enough to do that, it becomes cheaper to start at A and go to Z than it is to filter through which pieces you want to do.

There are two components to the application process that I think need to be made, though. One is, and David Kingsbury made this point, you need to integrate whatever is done in the way of technology development and developing new tools, you need to integrate that very well into the ongoing basic research that's going on at NSF and NIH and at DOE.

And certainly that's something that probably—NIH is just a gem of an institutional innovation. I don't think there's any institution anyplace else in the world that has been as successful at developing biomedical knowledge, and so I think we can feel confident that that part of research is going to go on very rapidly.

There's a weak point, however, in American policies, and that's the other place where this could be useful, and that is in the area of commercial exploitation. And I gather that, from look at your bill, that's one of the things that you would like to improve. And I think perhaps we should, in the next few hours, think a little bit about what institutional innovations we might think about that take advantage of our existing strengths at DOE and NSF and NIH, and think about how to push that out into the commercially exploitable sectors, how to integrate thoughts from private companies, how to incorporate strategic planning in the corporate sense into research planning when you're talking about constructing

tools that would be used by the companies that already exist in the biotechnology sector.

And I think that's a weak point and that's something that could certainly bear improvement in federal policy.

Senator DOMENICI. Doctor, I notice that in that very brief discussion you had a series of nods. [Laughter.]

Senator DOMENICI. For the most part, they were affirmative, but I noticed at one point a slight negative nod. Were you falling asleep or were you intending——

[Laughter.]

Dr. DELISI. No, he's quite an exciting speaker.

Senator DOMENICI. It was on the Japanese, where it seemed to me you might have had a——

Dr. DELISI. That's a good place for a distinction, the Japanese are not, their goal is not to try to sequence the human genome, but in fact it's similar to the goal we have in the first phase, and that is to develop technologies that would make sequencing a lot more, a lot quicker than it currently is, in fact we can do that, we can do comparison between horizontal studies. That would cost a dollar a base, and if you want to sequence a hundred thousand bases and twenty people and compare their sequences and understand disease susceptibilities, you can't do that, it's not a clinically viable procedure.

We can make that a clinically viable procedure. That's the goal, it's not to sequence the human genome, at least initially, as Bob mentioned. I think it's a nonissue in a sense because I expect in the next ten years we'll have the technology which will allow it to be done very quickly and relatively inexpensively.

And of course we don't know what we're going to find, and that's what science is all about. I mean, we're building the SSC and spending $4 billion and nobody knows what they're going to find. But you do it if you want to make progress.

In this case, it's not very expensive, or it won't be a very expensive thing to do, we'd be crazy not to do it, I think, at some point, but not right away.

The question—and of course, these technologies as they develop wherever at the labs, and the labs are going to develop, do high-risk innovative research. That's what the labs do. And when they make the—they do develop new technologies, they will certainly, I think will agree on this, we want to get them transferred to the private sector as quickly as possible.

The technologies are not just—I want to say it again, it's not just biological, it's not just engineering. There are computational techniques.

Dave Kingsbury said something, if we're going to drug design, one of the most rational approaches to drug design and vaccine development is through an extensive computational components to those problems, the National Labs have over twenty-six super computers in the system, it's the most powerful set of computational facilities in existence anywhere in the world, and there is a major contribution I think to be made here.

They are hard problems, and when they're solved, the capabilities will be transferred to the private sector and they will make enormous contributions.

Senator DOMENICI. Paul.

Dr. SILVERMAN. I want to comment we are tremendously excited about this revolution that you are predicting. We see it coming, but we also think that there's a concomitant development that has to go along with it, that there has to be a revolution in the way we actually do research.

I think that particularly in the biomedical area it has been often described as a cottage industry. And in fact the NSF, NIH granting systems, which are the envy of the world, tend to encourage individual entrepreneurship, people who establish their own niche, their own activity and establish their reputation, and except for certain program projects, in general that's the way much of the research has gone, and it has proven to be very effective.

This project, on the other hand, seems to require the integration of a number of disciplines, and Dr. Delisi very briefly alluded to a few of those, but surely engineers and computer types of a wide range of the spectrum, people, the theorists, that I've been fascinated or heard a presentation of the Los Alamos group and they brought physicists and laser specialists and computer specialists into focus on the problem.

I think people at Livermore and at our Lawrence Berkeley Laboratory are doing the same thing. I think the bringing into focus the support of the National Laboratories indeed is going to be, I think going to be a critically important factor in the way in which we enhance the rate of activity.

I also think that what Dr. Kingsbury has said about the need for us to be concerned about the expression of these genes and how one interprets that information, what are the factors affecting whether or not a particular gene does one thing or another thing must also be an ongoing activity.

And I hope that at no point in anybody's thinking is this activity of mapping and sequencing going to be an exclusive activity. It has to be supported by and imbedded within this broad context.

And as an example of that, I think that the selection of appropriate fragments and/or of chromosomes to work with as one begins the process will result in the production of a lot of useful information that will be immediately available for application.

And I believe that that is on everyone's mind and we are beginning to think and act in that fashion. So I think that this can—this is not—I don't see this as a period of a lot of hard work that's just not going to produce any short-term returns.

I think it's going to be a process that is going to produce short-term and long-term benefits that are almost unbelievable in terms of their potential application.

Mr. ANDERSON. First, I'd like to thank Senator Domenici for setting up this meeting. And as you in the audience must realize, we know each other and we would love to discuss technical issues for the rest of the day, but it seems to me that large science projects depend on public support, and they depend on the public understanding what the ultimate objectives are.

The space program had objectives that anybody could understand. The people who ran the program understood that they had to understand lane propagation, hydrodynamics of liquids in liquid fuel rockets, all kinds of technical problems.

They didn't bother the public with those. They set overall goals that could be generally understood. It seems to me that there's some fascinating ones here.

And the central issue is whether man can understand himself. Is the human mind sufficiently clever, are we sufficiently intelligent and can we organize ourselves well enough to understand how we are constructed.

That is as important as understanding the origin of the universe, which our space program is trying to tell us about, or understanding the structure of matter, which our high energy physics people are preaching to us.

Now, if you try to break this problem down, we find that we've got three billion base pairs which code for us and there are many people who don't think that's enough. There are more brain cells in the human brain than there are base pairs in our DNA, and those brain cells are wired up in an extraordinarily specific way.

So that many people have thought that there isn't enough information there to specify us, and a lot of theologians are sure that there isn't.

Senator DOMENICI. They're hoping. [Laughter.]

Mr. ANDERSON. On the other side, we have people who tell us glibly that it's mostly junk and that five or ten percent will do. How can we possibly stand to have such extreme views without finding out what the answer is?

Here we have the possibility of actually getting data that impinges on these problems. So there are philosophical, basic reasons for wanting the kind of information that is to be gotten out.

This is, as Dr. Kingsbury said, is all part of a general problem of finding out how cells actually work. And here we have a paradigm shift which is at the bottom of what we're doing. Until now, for technical reasons, not that we were—had blinders or had no imagination, till now we worked on one little thing at a time. Each of us would have his own enzyme or his own little thing to work on.

We're for the first time coming to grips with the true complexity of the system, with how many parts there are and with how they interact with each other. Why do we have to know that?

Well, it turns out that diseases such as cancer involve genetic expression and programming of the whole system. I think the easy problems have been solved. The most difficult ones now have to do with the analysis of a system, and it's stunning to realize that not only do we have DNA in us, we have over ten trillion copies of that DNA, made with extraordinary precision, so that every cell has a complete copy.

Well, we can go on from there to the spin-off reasons, the pharmaceutical reasons, the technological reasons, industrial reasons why we're interested in this project. But I think so far as the man on the street is concerned, to give these general concepts and then to say that here is the possibility that one shot of finding the cause of some 2,500 human genetic diseases is really stunning.

We're not talking about little increments of knowledge. We're talking about some big increments. And in the end, possibly they get us to what Lewis Thomas wanted us to get, namely, a way from halfway medicine, which is very costly, to medicine that is aimed

strictly at the cause of the disease and ultimately a cure, as antibiotics did for infectious diseases.

So, if I may present a personal view, a century from now, as history books are written, the big projects that were important in this century are the genome project, after it possibly space, and then the atom, and the order of those I don't know.

But the man who first proposed in the United States Congress to do this project is in history. [Laughter.]

Senator DOMENICI. Yes, sir.

Dr. CARRANO. Yes, I'd like to make a comment.

To drop back to the initial question that you raised, Senator, with regard to the benefits of mapping and sequencing, I think the two should be considered distinct. Although they work together very well, there are benefits that accrue from each and they're different.

Mapping can be done without any knowledge of sequencing. We don't need to have a sequence to do the mapping. It can be done independently. It can be done in a relatively short period of time, five to ten years, with a cost of somewhere between fifty million and sixty million. That's according to the best estimates that you've come up with.

However, sequencing can also be done without mapping, but it will be very cost ineffective. It can be accelerated by a mapping effort that precedes it or at least goes in conjunction with it.

There are also benefits, different types of benefits that accrue to each of those efforts. For example, the mapping itself, which is going on right now across the country, supported by many agencies, the primary effort is in the diagnosis of genetic disease, prenatal, postnatal diagnosis. That's certainly one of the first benefits that accrue from many mapping efforts.

The other benefits that accrue, particularly with regard to ordering strategies that allow one to take a map and to order segments of that map will be the ability to isolate genes of interest intact and to be able to study them, how they function, and what proteins they might make, so one can directly derive a protein without necessarily going through the genetic pool to get it.

Most importantly, it can help a mapping effort. An order set of clones can help primary ties, those sequences of DNA that we would like to—those genes in DNA we'd like to sequence first, prioritize our sequencing strategies.

Much of the controversy in this area has come with regard to, do we need to sequence the entire human genome. Maybe we do, maybe we don't. We don't have enough information now to know.

One could take an approach where knowing a map, knowing those genes that are the most relevant to the biomedical community, we can attack those issues initially and work on to the rest of the genome in time. So we can prioritize, given a map to work with.

Finally, there's something in mapping for the basic research scientists, in that it tells us something about domains of DNA, physical structure of DNA, how DNA is put together, and how these sequences might control the function of DNA.

So I think there are benefits to mapping that are important in their own right and should not be confused with any sequencing efforts.

Now, sequencing itself is also very important, in my estimation, and I think there are certainly benefits that would accrue from sequencing that would—that will be of interest to the entire scientific community and industry as well.

Particularly with regard to the operative sequencing, probably some of the most important things that would accrue would be the ability to have a gene sequence to use for, potentially for therapy, replacement therapy in the sense that now that we know the sequence of a gene, and one might be able to make in a test tube, that gene product is to be used in therapeutic sense, a pill or an injection, for example, to help alleviate a genetic disorder.

Secondly, at some time in the future it might be possible to design these genes for actually replacement in a living organism for gene therapy. But that's some time in the future.

So I think, as we go through these discussions, I would hope people would keep in mind that there are really two efforts here, a mapping and a sequencing effort. The two of them really do work coordinately.

Mapping is not dependent upon sequencing, but sequencing will be very, very much accelerated by the advent of the map.

Senator DOMENICI. Yes, sir.

Mr. OESTERING. Speaking for my small segment of the private sector, I would say that we could play our traditional role just to make the technology available in the form of diagnostic services or with therapeutics when that time comes.

And at our company we have in fact done that. We have started a reference laboratory where we offer diagnostic testing based on DNA probe technologies.

This technology is in its very infancy and it's in a very crude form. It's very labor intensive, takes a long time to provide an answer to a diagnosis, but we felt it was important to provide it and it was—that somebody should get in there and start doing it.

And I think, you know, the private sector will become more and more interested as the technology develops and becomes easier to perform.

I also—but I would also like to suggest that we shouldn't leave the private sector out in terms of the research that's going on. It was our company, scientists at our company, in collaboration with a group in Toronto, that found the location of the cystic fibrosis gene.

And the reason that we did that was because we had—we've made a commitment to this area for going on four years now, and we've developed an extensive panel of DNA probes and we've made very good headway towards a genetic map and feel that we're reasonably close to a genetic map that would be useful in attacking the more common diseases, at least from the standpoint of diagnosis.

So I think that the private sector could be included in the research efforts as well.

And speaking of the competition, I can say that in both—you know, outside of the United States, this technology is being tracked

very, very closely. There are seven companies in Japan that perform reference laboratory diagnostic services, like we are offering now in the United States. And even the genetic disease tests that we offer are not even—do not even occur in Japan.

Six of these seven companies have approached us and have—we are negotiating with all six of them to license the technology for them to use. The same thing is going on with the major diagnostic companies in Europe.

So there is—it's being as closely tracked as any other technology area that I've worked in.

Senator DOMENICI. On the first round, anybody have any other observations before we move to the next idea?

[No response.]

Senator DOMENICI. Do the different agencies have complimentary roles? Maybe we ought to ask you to start with that, if you would.

Dr. COOK-DEEGA. Sure. I think that——

Senator DOMENICI. I'm assuming in my notes that you're a neutral observer. [Laughter.]

Dr. COOK-DEEGA. Gosh, I don't know. I try.

I think that that's almost a perfect word to describe what DOE and NIH have been putting together. There's been a lot of press in the last year and a half. In fact, one of the funny things about this whole human genome initiative is the degree to which the science press has kind of gotten in the process and it makes it harder to set policy because, trying to formulate policy in a fishbowl, you don't quite know how your ideas are going to be played out. You're quite familiar with that.

But I think the degree of disagreement between the agencies has been magnified quite a bit by the scientific press.

My sense is that DOE's strengths are in multidisciplinary large group research that involves the National Labs, and NIH's strengths are in the small group research initiated by investigators.

And those are complementary strengths and when you're talking about doing something in the nature of tool construction, it seems to me that you want to do two things. One, you want to make sure that the people who are going to be using the tools have good research support. So you want to make sure that small group research is supported and that this doesn't detract from that kind of work.

Second, it seems to me that you're probably going to have components, some—you're going to want new ideas to be percolating from the small group research as a part of the human genome initiatives, and other things are going to—you just can't design a DNA sequenator with two people in a laboratory, it's just not the way it works. You need expertise from too many different areas to do that.

And a lot of the technologies that are the most innovative in sequencing and mapping, all that, the automation, they involve many, many different disciplines. And that is an area of strength of the National Labs. It's also an area of strength—I think the National Lab strength is really taking high-risk, long-term research, bringing it a certain distance towards development.

And I think at that point there's a very big role for private industry to insert itself, take promising technologies and commercialize them. I think that's a step where we're stumbling quite often.

But frankly, I think that the current coordinated efforts—there is an agency that in fact—David Kingsbury started the ball rolling, at the cabinet level there is a working group that involves the Department of Energy, NSF and NIH and a couple of other agencies.

They're already talking, there's—as you've heard, there's informal interchange of personnel, and in fact there's been a lot of telephone contact. So I don't think coordination among the agencies is a serious problem.

I think more important is what doesn't exist right now is any concerted efforts to strategically plan the different efforts. One of the things that I've been hearing quite emphatically from the scientific community and from the industrial people that we talk to at OTA is that there's no sense of knowing quite who to talk to when you're trying to figure out what should be the components.

And I think one of the things that was attractive about your bill is that it seems like there was a focused mechanism for doing that. I don't know whether it's the ideal mechanism, but I think there is some role to be played by an outside advisory committee that either involves the government or doesn't involve the government.

But I think in terms of what's happening in government now, the coordination efforts, I don't think much needs to be done there.

I think what we need to be thinking about instead is how to set the agenda for the federal agencies rather than worrying about any squabbling or whatever. I don't think there's been very much of that. What there has been of petty squabbling, I think is caused by DOE and NIH both thinking they're the best agencies to do what they do, and I think they're both right. [Laughter.]

So I really don't think that's—I think it's a nonissue. I think the more important issue is how do you structure it so that the private sector can play a role in strategic planning and how can you involve outside scientists in setting the agenda for what the agencies do.

Dr. KINGSBURY. You want me to report on the—I don't remember, some months ago, I've lost track of time——

Dr. KIRCHSTEIN. Last spring.

Dr. KINGSBURY. It was last spring, the Domestic Policy Council asked the working group on biotechnology to assist them in helping derive the administration's policy toward the development of this project and dealing with the different agency interests.

Part of this was stimulated by the fact that things were moving very quickly. Part of it was stimulated by the fact that the press was painting, as Bob has just said, a very interesting picture of agency guerilla warfare which none of us in the agencies really quite had experienced, but it certainly was there.

There was some questions about setting priorities within this project, how big should it be, how quickly should it move and who should be involved in it. So the biotechnology working group at the Domestic Policy Council took this on and we dealt with it as a subset of that, or we put together a subgroup.

Since the DPC is made up of agencies which have no—have some direct interest as well as agencies that have no direct interest in

this, we decided to focus down on the agencies that had direct interest, formed a subgroup, and that subgroup then developed some basic information.

And I think Bob has just described rather accurately the determination that we came to, is that I think we all recognize that this is a very broad project when it's taken in its entirety and that within the agencies that are most directly involved there's a complementarity rather than a competition.

There are areas of overlap. There's no question there are broad areas of overlap. But those areas of overlap are at the boundaries of certain kinds of activity. An example is the fact that the National Science Foundation supported the development at Cal Tech of the current DNA sequenator that's pretty close to the state of the art.

That DNA sequenator, God bless it, is a nice machine but it doesn't quite do everything we want it to do, and the people at Livermore and people at Cal Tech now are involved in developing the next generations and new uses for that, clearly complementarity between NSF and DOE.

You've already heard a report about the efforts in terms of computer base, data base development that goes on between NIH and DOE and NSF. So there were clear areas of complementarity and overlap.

Other areas where DOE was very critical to developing a set of reagents that were going to be of great value to the NIH investigator community. DOE does not have that investigator community that it deals with. And it's not—really, it's missioned to do that. NIH does have that community.

Many people at the NIH who are current grantees or the intramural people would use these ordered cosmic clones that are going to be developed at Livermore and use them extremely well and very fast.

So it's very clear that this project had a broad base, very narrow areas of overlap, but some overlap, and a natural sort of development. And the agencies were going to cooperate very well.

We felt that that mechanism, that committee that was developed functioned quite well, and that we were very satisfied with it. We have proposed that we maintain that as a coordinating mechanism into the future.

What base it comes under and what form it ultimately takes was not determined. Right now we can do it within the framework of the existing committee structure.

It was important to us, I think, that we did not view a lead agency. We stayed away from that. There was no reason to, because of the nature, it was essentially a revolving leadership. And it gave us a chance for coordination, it gave a chance for priority setting without having a focus of leadership that really fell in any one area.

In my perception, from all of this, and maybe since every other agency is here they can correct me, but I felt that as we had moved on in this project this was a comfortable situation.

The rotating chairmanship that had been agreed on seemed to be a very rational and functional way to proceed. And, yes, there is a place now where letting the scientific community know what we're

going to do, interfacing better with the private sector is something that needs to be done.

This has been a very rapid process. We are now talking about developing scientific—science policy in a relatively short period of time, considering the nature of this project. I don't think any of us are fully agreed that we fully understand how quickly we can go.

As Charles has said, if Los Alamos does its homework well over the next—maybe sequence the whole thing in a year and then all of our policy goes right down the——

[Laughter.]

Dr. KINGSBURY [continuing]. Wherever policy goes. So I think that the—we felt quite confident that this kind of a coordination mechanism was going to be the most effective, but that clearly a broader base of getting the scientific community and getting the private sector in was our next step. And that mechanism we don't have in place yet.

Dr. KIRSCHSTEIN. Senator?

Senator DOMENICI. Yes, Ruth.

Dr. KIRSCHSTEIN. One of the things that took some time was to have the group, the subcommittee under the working group of the Domestic Policy Council actually develop the information about what all of us are doing, because our scientists working at full tilt have not always answered questions when they've been asked as rapidly as possible, nor do I think they need to, because we really do want them to work in the laboratory.

But I think we finally do have the information about what all our free agencies and some of the private sector and some of the scientists supported by a number of private foundations and groups, Howard Hughes Medical Institute is a very big player in this, and we had to find out what it was supporting, American Cancer Society, American Heart Association, et cetera.

We have that information now and we think that making it available, which Dr. Kingsbury is about to do, I think——

Dr. KINGSBURY. Yes.

Dr. KIRSCHSTEIN [continuing]. For everyone, will help to have coordination and will help to answer the questions when scientists call as to who is doing what. And so, it's really moved quite rapidly.

Senator DOMENICI. Any other comments on this?

Dr. Delisi.

Dr. DELISI. I basically agree with everything that's been said. In fact, it's impressive how well the agencies——considering the complexity and the speed with which this is developed, how well the agencies have communicated. And I think that's what's needed.

Coordination tends to me to imply some type of oversight, somebody saying you're doing this and you're doing that. I think we need communication, and we've got it. Ruth mentioned a personnel transfer before. Dave Kingsbury and I are co-chairing the NSF-DOE committee to coordinate on the human genome.

We're also thinking of co-funding centers, so there's a lot of communication between the agencies. And I agree with Cook-Deegan, I think the important—the really important issues now are to get on with trying to determine how to structure this so that any innova-

tive technologies can be transferred as efficiently and effectively as possible to the private sector and to the universities.

I think that's really the crucial question here, to really make use of what comes out of this as quickly as possible.

Senator DOMENICI. Anybody else on this issue?

[No response.]

Senator DOMENICI. Well, maybe we ought to move on then. Why don't we do this, I think it's a good idea, just let me make this observation, and then we'll take about a five or ten minute break, and we have two more general issues to resolve, three I guess, and then anything else you all would like to do.

Frankly, I am--I think you all who work within the White House and who are part of the executive branch's either general group in the area discussed or more specific, Dr. Kingsbury, as you indicated you pulled it down, somehow or another, if you don't mind, since we're all being very, very frank, I'll give you my frank assessment over the last year and a half or two.

Frankly, I hear a great deal about all this coordinating that goes on in the White House with reference to science initiatives, competitive initiatives, and I really am not great at analogies, but you know, what I hear that's been going on and then what I see born from it, really don't match up at all. I mean, I frequently think, since it's a Republican White House, that an elephant is going to be born, and I see a gnat. [Laughter.]

Senator DOMENICI. You know, if anything—I hate to say it, but with reference to super conducting materials, regrettably, I believe the White House was given some great ideas, spent a hell of a lot of time with very bright people and called a great big, marvelous national conference, and I'm not at all convinced that they gave birth to much. You all may disagree, but I really do—that's my general feeling.

And I think that's understandable, because I really believe that as great as your agencies are, and yours is magnificent, and obviously DOE, since I've been called the senator for Los Alamos, I must think it's great. [Laughter.]

Senator DOMENICI. But frankly, I do believe the urgency of new arrangements in the world we live in, for lack of using those other words, people always talk about consortia and joint venture, I'll just be general and say new arrangements.

The urgency seems somehow or another to either be lost in the Federal Government or we are in a situation where it is most difficult, if not impossible, to make new arrangements occur.

And I think our competition in this world, whether it is as you all have described it with reference to this process that we're describing, I think our difficulty worldwide is that others have made new arrangements and they're not suffering from them as we are.

And I don't believe the Japanese come anywhere close, per capita, spending the money on research that the United States of America does. In fact, you can strike the word believe, I know they are not. And they are somehow or another, and I'm not trying to—in the parlance of today's meeting, clone the Japanese. [Laughter.]

Senator DOMENICI. But basically, they are getting more for their dollar in research than we are, and that probably means nothing, except the reality is, if it just meant that we were spending more

and they were spending less and isn't that neat, it's a reality and a fact if there was nothing else coming out of that, that would be all right.

But I'm afraid spending less, some other countries are getting more, and I do not believe—more in the applications now, is what I'm talking about, that you have raised even here, that our next most complicated and difficult area is to get—how do we marketplace orient in some structured way this research.

I think that is generic to the Department of Energy, and since I am not as familiar with your institute, except to say I have heard from some, some say it is endemic to your—to the National Institutes of Health also, that those in the delivery system of health care would say that there is a very, very significant gap between the dollars spent, the research being done, and the marketplace availability, and I know that's the case in some other arenas, Department of Defense in its research, although I would tell you for all the criticism of the Department of Defense research it moves into the private sector quicker than some of these others.

Now, that may be natural, because ultimately the private sector builds something for them, but they don't even covet their research as much, it seems like, as some of the other institutes, that it's theirs and we're going to wait around and make sure that it is not something very, very special and secretive.

So I would close on that note, and we'll come back and talk about whether there's anything to that and how we ought to think about the private sector involvement in this. But first we'll talk a little bit more about whether there are any new arrangements necessary by way of policy decisions between the different involvements in the Federal Government.

Let's take a brief recess.

[A brief recess was had.]

Senator DOMENICI. If we could just take a break from our normal agenda and ask—first, let me tell you that Dr. Kingsbury has to catch an airplane for an urgent meeting in the morning, and we understand he has about three or four minutes and then he must leave. I have asked him if he might just make a few summary remarks before he leaves, and I want to thank him in advance for the effort of coming here. I appreciate it very much.

Dr. KINGSBURY. Thank you. I suppose I should rise to the defense of the Domestic Policy Council, but I won't. [Laughter.]

Senator DOMENICI. That's all right; whichever you prefer.

Dr. KINGSBURY. Certainly, coordination of policy is a difficult issue at all stages, since we have got multiple tiers and those of us in the agencies need to coordinate with the people in the Senate and the House and with different agendas, that's always difficult.

I think in the sense of a summary kind of set of comments that I would make, is to again stress the fact that we're moving along well in terms of getting the kind of communication between the government funding agencies that's necessary to keep the project in a reasonable focus.

I think we understand each other in terms of what we're trying to do. I think the mechanism for doing that is straightforward.

I think where we're falling down, an area that I would hope that you can focus on in a meaningful way, that you've addressed in the legislation, is this technology transfer aspect of things.

That's a difficult issue always. I think that we've been trying to find ways of doing that with university research, with government laboratory research. The National Laboratories clearly have become aware of this problem in recent years and are trying to do something.

I don't think any of us fully knows the answer to doing that kind of technology transfer. One of the ways that we at the National Science Foundation are attempting to do this is to establish programs in which we have made provisions with, as research centers, so that up front the research is shared with the private sector as partners.

I think that's a very effective mechanism to move ahead. I think we've seen some beginnings that that kind of partnership is possible. Certainly, forming those kinds of partnerships with the National Labs is something that is developing within a few of the laboratories, and I would like to see that expanded.

How we best do that and coordinate it at the federal level is something that I won't attempt to answer. I think the proposal that you have for a broad based body of advisors that includes representatives of the agencies, the laboratories and the private sector may in fact be an effective mechanism for beginning this.

I think the one thing that I would caution, however, is that as much as we'd like to think that those of us in Washington are very effective, and of course, we all recognize that we are, it's the individual scientists in the laboratories talking to the individuals in the companies that is even more effective.

Senator DOMENICI. I agree.

Dr. KINGSBURY. And what we really need to do is find a way of enhancing that kind of scientist exchange mechanism to open up the National Laboratories and to support research laboratory center support that encourages people from the private companies to come into those laboratories and work and provides mechanisms for people to go from those laboratories into the private sector companies and work without fear of some kind of a conflict of interest, other kinds of proprietary problems.

I think that if we were going to focus on the most effective mechanism over the short period of time, it would be some kind of a mechanism for scientist exchange and opportunities for companies to come in.

With that, I thank you.

Senator DOMENICI. Thank you very much. I'm most appreciative. And if I have anything further to say about the council, I'll ask her to excerpt it——

[Laughter.]

Senator DOMENICI [continuing]. And we'll send it to you special delivery.

Thank you very much.

Let me just follow on with that and ask if the National Lab representatives who are here, if they would comment on how they see the role of the National Labs, since we have you here with refer-

ence to frequently looking at the overall picture of technology transfer.

Let me give you my version of why I know the technology transfer, whether it's an exchange or knowledge that we described, or whether it's counting patents and licenses, whichever you want, why I know that the Department of Energy's technology transfer in that concept is not working.

Frankly, if you want to take a cross-section of CEO's across the country that are people involved in research, spending a lot of their money and time and have their future at stake, if you want to just run a national survey, I would just gamble on my little sampling that you will find a tiny, tiny number who are aware of what's available right now; forget about further improvising the royalty laws, a tiny, tiny few are aware of what they could get out of just using the labs now.

And that's my first observation, and I think that means something is wrong, and I frankly believe it is very simple. In the American marketplace, businesses large and small do not spend their money on things, at least not intentionally, though they waste plenty of money; but they don't spend their money intentionally where they can't expect benefits and results.

And I actually believe we have set, to this point, and there's a change in attitude and there's a lot of things happening that are exciting, but I think there was a general feeling that it was futile for them to try, that they could get nothing out of it, the few that did try.

My goal is to broaden that some way, so that—and it may be through the exchange of people, that may be the starter. Dr. Kingsbury might be right. But I also think the labs have to take some chances in terms of new arrangements for joint type research efforts.

Universities, except for a few of these big labs that the government runs, and except for a few universities, are not intimately involved either. They're involved, but not intimately, maybe Firmi's the best with a relationship with six or seven, and I think that's a shortcoming, too. I don't have a fix for that, but I sense that it is a shortcoming of a different caliber.

And what's happening is, as a consequence—I'll conclude—and then I'll shut up—is that the National Science Foundation with its centers of excellence that it's funding, is going principally to universities and private sector firms and forging a relationship.

Frankly, I think, in a couple of major, major areas that's rebuilding a house. I think they left out a house by not centering them around some of the laboratories and moving out from them. But I don't know how to do that either except the way we've been doing it. We've been pushing them.

National Science Foundation, I've got to give them credit, they are at least verbalizing it and they're not precluding it in their centers, in their thesis on centers where they're talking about centers of excellence, they're not leaving labs out anymore, Doctor, are they?

Dr. DELISI. No, they're not.

Senator DOMENICI. Now, a couple of years ago they were a little squeamish about it, and I don't know who caused that.

Dr. DELISI. This is a concept we've been interested in for the past year and a half, or that is, I've always felt that the university private sector centers that NSF had left out a very important part, as a third component to the scientific community, and that's the National Laboratories, and David Kingsbury has in fact agreed that we should indeed have ternary complexes, and we've discussed some specific proposals.

Senator DOMENICI. Now, can the people from the National Labs involved here tell us how they see their role in this project and how they see some impediments to current arrangement, whoever wants to go first.

Go ahead, Doctor.

Dr. CARRANO. May I submit to the table a document you may want to keep for your records, which discusses the current role of Lawrence Livermore Laboratory in physical mapping effort.

I believe that our program and most of the programs at National Laboratory emphasize two aspects, the multidisciplinary nature of the project and the high risk nature of the project. And that's where our strengths lie.

Senator DOMENICI. You have to speak up so that she can get this. I'm not just saying this for you, she has reminded me before, Doctor. Thank you. I forgot to mention it.

Dr. CARRANO. With regard to the physical mapping and sequencing effort at Livermore, I can address these two in a little more detail.

The physical mapping effort that we've initiated at Livermore really is a multidisciplinary approach. It involves many components of biology, it involves basic cell biology, biochemistry, recombinant DNA technology to touch across the biological field. But that has to be blended and cannot exist alone. It has to be blended with other disciplines.

Heavily involved in our effort is a computation program. We require both software solutions to address some of the biological needs, and we require some hardware solutions. We requite data communications effort.

The energy sciences network which is being established probably with a focus of Livermore branching out to all the National Laboratories and other institutes could serve as a backbone for communications and networking in this regard.

So there's the biological, there's the computational, and in addition, there's an engineering effort. There is a tremendous need for instrumentation development and laboratories have had a history in terms of unique instrumentation development and support of biology in particular.

For example, the flow systems technology was developed at Livermore and the Los Alamos National Laboratory and pioneered by both laboratories in the national gene library project.

The instrumentation that's needed for this project involves automation of biochemistry laboratories and automation of techniques to separate DNA fragments.

The engineering staff are there to do this, design work can be done, and the staff is there to put the components together.

So I think with regard to the mapping effort, at least in our effort, these are there at the laboratory and it works well together because we're in a matrix system.

Most of these needs for any one of these areas fluctuate and not in regular cycles. This month we may need the emphasis of two engineers. Next month they may go away and we need a biochemist.

And so we can cycle through the matrix to divide the needs as we demand them. And that's strength, because of the matrix organization of the laboratory.

The other area is the high risk research. New techniques are needed to accelerate the program. We can do the mapping and sequencing effort with current technology, but that would be a long-term effort and costly.

We need to develop some new approaches, and they are risky, and getting agencies to accept the concept of an approach that may not pan out in the past has been somewhat difficult. And the National Laboratories have gotten involved in some of this high risk research.

For example, at our particular laboratory, developing strategies to put clones together, we're developing a new chemistry to do that. We had no idea it was going to work, and in about six months time we have done a few principal experiments to show that it can work. And I think now that can attract more interest and more funding.

So I think the high risk aspects of these things are an important component of doing some of these projects at the National Laboratory.

Senator DOMENICI. Thank you very much, Doctor.

Dr. BELL. In thinking about the possible roles of the National Laboratories, I find it useful to reflect on the various kinds of activities that are going to be required for a project of this sort.

At one extreme, if you will, why, we have sort of individual investigator initiated projects which are typically handled by a grant mechanism, let's say NIH or NSF, and these are characteristically, although not exclusively, at universities and they have a subsidiary aspect of training students, which of course is important.

Even this sort of thing can have a component at the National Laboratories insofar as they may be engaged in basic research on a small scale. And I'll give you an example in just a moment.

Then at sort of an intermediate or larger scale, why, we've heard that technology development centers which can combine interdisciplinary resources of a major research and development organization, such as the National Laboratory or possibly a major biomedical research center, can certainly play a very important role, particular in applied research and process development.

And it seems to me that here there's certainly a great deal of scope in principle for involvement of the university, contributors at early stages in these process development considerations, and industry maybe all along, early, late, which we've been somewhat deficient in, pilot projects jointly with industry and National Labs and others.

There's a third kind of technical activity which probably will be the most expensive in this sort of project, which I think has at least three components. One is that there will have to be an infor-

mation resource and communication network wherein all the information that's developed in the mapping and sequencing activities is, if not brought physically to some centralized place, at least from the point of view of the user of the information, is brought into a centralized and readily accessible form so that everybody can dial up using their PC and find out precisely what the status of mapping of some sequence, or some chromosome area or what sequence information is known.

And that obviously has to be a highly centralized and coordinated activity, whether it's physically in one place or not. And there I think it's very natural to think of a collaboration of National Laboratories and industry handling that sort of thing.

And I should remark here that the GenBank operation which has been funded under the management of Ruth's institute and with contributions from DOE and NSF and several other of the National Institutes of Health, has in fact been a collaboration between Los Alamos National Laboratory and Boltmer, Addington, Newman, which is a private company. And in addition, the European Molecular Biology Laboratory contributes to the assembly of the data.

And then the further distribution of the data is handled by innumerable private biotechnology companies or other companies that distribute the data with their own software and maybe their own hardware even.

That I think in a very small way is sort of a paragon for a way in which collaboration can be carried out, using some resources from the National Laboratories, some resources from industry, some from universities.

Okay. That's one sort of centralized activity.

Another centralized activity is going to be the clone repository, that is, all the clones that result from the mapping exercise are going to have to be available to people who want to use them, and presumably one wants to put them all in some place that specializes in this, such as the ATCC, American Type Culture Collection, which I think is a private organization.

Mr. ANDERSON. Nonprofit.

Dr. BELL. Nonprofit.

Dr. KIRSCHSTEIN. Supported very heavily by NIH.

Senator DOMENICI. Foundation?

Dr. KIRSCHSTEIN. Nonprofit foundation, with a profitor attached to it.

Mr. ANDERSON. Which we are associated with.

Dr. KIRSCHSTEIN. Right.

Dr. BELL. So anyhow, this is going to be something that's going to have to be done in a highly coordinated and centralized fashion, probably some private arrangement is the most reasonable and cost effective for that.

And then there have to be things which I would call sequencing factories, that is, places where their business in life is to determine sequences that other people send them, basically, as rapidly, efficiently and accurately as possible.

Now, probably the sequencing technology is going to be developed at these technology development centers, and whether those happen to become involved in the factory aspect is a detail, per-

haps, but I would think that this service would primarily, probably be offered by private industry, obviously, for a charge.

But it would give them a strong capability in offering that service to anybody in the biosciences that need it.

There is a fourth kind of activity which is separate from the foregoing technical things, and that is program direction which it seems to me if you have a goal oriented, long-term program, you need a single place where program direction can be—where the accountability for the program direction can be levied.

And obviously it has to have all kinds of ways of getting advice concerning the technical aspects of the program from the scientists who will be the ultimate users, and they should be important in giving input as to priorities and schedules.

You obviously have to have coordination with all sorts of related activities, but it does seem to me that you really need some accountable organization that is responsible for the program.

In principle, that could also be a National Laboratory. It could be something else, too. But I don't think it could be a committee.

If we turn to the specific example of what Los Alamos, as a National Laboratory, has been doing in some of these things, I've mentioned the GenBank activity, which has involved collaboration of private industry, and which is largely funded by NIH, although it's conducted at a DOE installation.

We also have a national research resource for all sequences related to the AIDS virus, which again is totally funded by NIH and it's carried out at Los Alamos, using our computer facilities and GenBank's capabilities to study the mutation rates, the scope of viral variation that is seen.

We also conduct research at sort of the individual investigator level, concerned with, for example, pattern identification in genetic sequences. If you have a long sequence, how do you determine what parts of it, knowing nothing else about it, code for protein, what parts are information concerning the regulation or the expression of that piece, what parts may be for structurals.

Well, we don't know those answers. And one approach is to try and use artificial intelligence methods to take the protein coding parts, and we have some people doing some very basic sorts of research along those lines.

The third activity which gets generated by this sort of interdisciplinary approach is we think that training is also an activity which is provided through GenBank.

We employ six to eight graduate students, typically, for a year or two at a time, and they come and if they know something about computers, then they learn something about molecular biology in order to apply computer technology to organization of the data base.

If they know something about biology, then they learn about computers. And when they return to graduate school or medical school or wherever they're going, they're very much in demand as resources who are familiar with the GenBank data base, who understand something about molecular biology and more than most of their colleagues about how to analyze it using computers.

Similarly, in the—so the things that I've spoken of so far at Los Alamos have had to do more with the computational aspect of

things, which is my own specialty and background, and the physical and biological business, I think also the interdisciplinary capabilities of National Laboratories are important.

Tony touched on the contributions which both Los Alamos and Livermore have made to the flow cytometry or ability to sort chromosomes now.

The technology that Charles Delisi referred to as potentially leading to much more rapid methods of sequencing is sort of an extrapolation of this to try and detect single molecules in the same sort of apparatus by refining the sensitivity as far as possible.

In the laboratory we also have activities in robotics, which may be very useful in DNA sample preparation steps for the sequencing activity. And all of these things are sort of straightforward in a National Laboratory because of the interdisciplinary character or the—Ton referred to it as a matrix sort of setup if one can people with diverse backgrounds and interests.

And I must say in a project with the vision and scope of the human genome one, it's very easy to find people that are very excited by the possibility of participating in an enterprise of this sort.

Senator DOMENICI. Thank you very much.

Dr. SILVERMAN. I would like to add to what both Tony and George have said about the National Laboratories in terms of both underlining the multidisciplinary and multi-investigator nature of the problem and how effectively this can be done through the matrix organization that Tony has identified.

I'd like to add to that, however, and indicate that not only within the laboratories is there this kind of multidisciplinary, multi-investigator approach, but through the Office of Health and Environmental Research of the DOE we have been and do regularly meet and coordinate and talk about our activities.

So we already have a structure in place that I think is working effectively. And in fact the last months have been characterized by a series of meetings that have in fact led to agreements or arrangements between us to work in various ways in complementary fashion.

So there is in fact a subset organization that could be in place that ought somehow to be recognized, and the board holds of that is I think identified in the bill. And I think that needs to be kept in mind because perhaps the awareness of that is not perhaps as much as it ought to be.

With regard to the Lawrence Berkeley Laboratory, very specifically, because of our long-standing interest in radiobiology and radiotherapy, we have had a long interest and this has evolved into both a molecular and cellular approach as to how the human genome is affected by factors that are certainly derived from radiation but also nonradiation effects, such as pollution.

And so we are concerned and have been with mutogenesis and carcinogenesis. As a result, we have a very substantial group of molecular biologist.

And the other aspect of this is that we are in very close proximity, we share a campus with the University of California at Berkeley, at any one time to emphasize the training aspect of this, we have between seven and eight hundred graduate students in vari-

ous parts of the laboratory undergoing training and contributing in various ways.

It also provides the kind of context within which one can really attract top-notch people from around the world, and I think that we collectively, with the campus, have been able to do that.

And I think it is also important that one of the major spinoffs from the system that has developed there is the development of the world's largest collection of biotechnology industries in the Bay Area.

Between Stanford, UCSF, San Francisco, and Berkeley, this has evolved a very unique capability that I think not only can benefit from but contributes to, in a very significant way, the development of the science.

It's important in those, Tom's comments were very interesting because some of the most recent, most important publications that have come out in the field of molecular biology and the identification of specific enzymes, their localization, the cloning, and so forth, has come out of an interaction between biotechnology companies and universities.

In the Howard Hughes, and so forth, these are papers—in the old days there used to one or two authors on a paper. Now if you have less than eight or ten, you know, that's remarkable. It's usually twelve or sixteen authors, and it's a collection of various institutions which are contributing to this development. And that's part of the cultural exchange which I alluded to previously.

The Human Genome Center at the Lawrence Berkeley Laboratory is headed on an interim basis by Robert Mortimer, who is the chairman of the biophysics department on the UC campus, and holds a joint appointment in the laboratory.

And his international reputation has been built on the genetic mapping of yeast. And this is—it's a diploid cell, it's an appropriate model for a human cell. And as a result of the capability that they have developed at Maynard Olson at Washington University and Mortimer, they are able to take component fragments up to a million base pairs in size and create many chromosomes.

And by doing that and replicating them in the yeast cells, they will be able to build up a library and carry out a reordering of these fragments much more rapidly than the previous technology was capable of doing, which was only 40,000 kilobase limitation.

And in fact it is that technology which we are sharing with Livermore, for example, in a collective effort to use that to map human chromosome 19, which has a number of very important genes on it.

So these things are in effect and they operating. In addition to mapping and cloning, we also have one component part of the Human Genome Center which is concerned with understanding the structure and function of both nucleic acids and proteins as derived from the kind of genomic information, and that's what I think David Kingsbury was alluding to and Ruth was alluding to, that we need to know how this information is translated into a functional biological entity.

And so that is one component part of our work and that again is a collection of individuals both on the campus and in the laborato-

ry, and also using, accessing of the capabilities that are available in the biotechnology industry.

In fact, we have one person who works half of his time in Genentec and half of the time in our lab, in order to share and exchange information.

And finally, I think the general translation of that information into a final product, gene expression, is a very active activity that is ongoing, both transmembrane signaling and the whole transfer of information and how that finding results in a product which is expressed, there again that's a major aspect of our energies.

I think combining that with the capability, and we trust that this will be a new additional capability, not competitive with any of our other work, that there will be new funds available, to put it bluntly, and not just redirection of the other energies.

I think that in that environment and with this kind of coordination, I think the National Labs have the capabilities of making a very significant contribution to this total effort.

Senator DOMENICI. Anybody want to comment on that?

Mr. ANDERSON. Could I make a comment?

Senator DOMENICI. Sure.

Mr. ANDERSON. This is from some 30 years in National Labs. What's unique about them is seen in practice, the ones I've been were organized by discipline, so one belonged to a group that was in his discipline. And then traditionally, when a big project was done, people were split out to build a reactor or do some such thing, into a separate group and then had a place to go back home.

Now, that meant that you had available minds from different disciplines. I've never seen anything akin to that in a university, ready availability of people with very different training.

For example, I have had assigned to me a hydrodynamicist from the reactor project to solve a problem we had for six months. The top theoretical person in the gases diffusion plant was available for a certain amount of time. I had some problems in crack propagation in rotors and some very good metallurgists were available to work on that.

If I tried to do that in a busy university, where each professor has his graduate students around him, it would take a very long time to get organized.

So there is something here that has been extraordinarily unique, and that is a certain flexibility to use people across disciplines, to get them interested and to use them. And I don't think that that gets across very well. You have to experience it to find out how it works.

Senator DOMENICI. And your experience was at Oak Ridge?

Mr. ANDERSON. Yes.

Senator DOMENICI. Well, let's move on. Can we just talk a little bit about the current environment for collaborative research and technology transfer. Is it what it should be? Should the private sector, in discussing that, have a role in planning the priorities of the research?

Let's take the two together. I've already expressed myself and perhaps in a biased manner without knowing enough about the first one. I don't believe in the current environment collaborative research and technology transfer is all what it should be.

I'm looking for better ways, and I think everybody else is, too. I'm concerned that some of the institutions are too busy doing other things, but I think they're beginning to understand that they're very vital to our future.

Could you address that? If you feel more comfortable addressing the second part of it, should the private sector be involved in the goal setting and the policy making, if we're going to try to do that, either one or both of those.

Ruth.

Dr. KIRSCHSTEIN. Senator, for many years, in the thirties and the forties, early fifties, the chemists at the universities throughout the United States had excellent working relationships with industry.

They were able to patent materials, and these were quickly turned into products.

Biologists, medical biologists, nonmedical biologists, agricultural biologists, had never done such a thing, but they've learned, and they have learned extraordinarily rapidly.

And almost every molecular biologist at a university throughout the United States, and indeed the scientists working on the NIH campus, government scientists, now have developed interrelationships with the small and sometimes large biotechnology industrial components all over the country.

There are patent agreements that are being made, recombinant DNA was patented by Stanford and licensed out to companies, Stanford and the University of California, I believe, in San Francisco, so that the biologists have come of age in this in a way that chemists knew a long time ago.

And I think the very fact that the cystic fibrosis marker was worked out with a company along with the university people in Toronto, this was, it could have been in the United States and there are others working in the United States, shows that biologists have done that, even as I say, the intramural folk at NIH.

One of the reasons, for example, that the drug AZT became available as rapidly as it did for treatment of AIDS victims was because of this kind of collaborative work between scientists intramurally at NIH, Dr. Robert Gallo, and the Burroughs Welkin Company.

And so I think that what is needed is a continuation of what has started with perhaps the kind of thing you've been talking about, some further impetus to make it more orderly. But I think it's on its way.

Senator DOMENICI. Anybody else?

Dr. SILVERMAN. I worked in both universities and more recently in an energy laboratory, and as you know, the University of California is now discussing with the Department of Energy its new contract. I think you're made aware of some of the issues involved.

Senator DOMENICI. Yes, sir.

Dr. SILVERMAN. And there's clearly a disconnect between what it is we are supposed to be doing and the people who are negotiating the terms of that contract.

We are frustrated. We have many, many relationships, our material science people have exactly the same kind of relationships that Ruth has just described. We have science advisory groups from the private sector.

I personally believe it is important for the private sector to be involved at all stages, at all levels of policy making and implementation.

Our relationships with the biotechnology industry have been nothing but favorable, and we have benefited and I think they have, but we are now being asked, through these contract negotiations, in effect, to step back 20 or 30 years.

Yet we hear about the need for there to be technology transfer or to be involved in many ways, and I don't know whether Charles has something additional to contribute to this, but I know that from our perspective we are very frustrated about this disconnect.

Dr. CARRANO. I'd like to also add, at the level of the individual scientist and at the industrial level, there is no problem getting the two groups together. Our problems are particularly when they come to putting them down on paper and getting that process completed.

We have two issues that are being hung up right now somewhere because of—somewhere in the system that just won't go through.

Senator DOMENICI. Now, yours is university?

Dr. SILVERMAN. We're under the same contract.

Senator DOMENICI. And you are——

Dr. BELL. Sandia.

Senator DOMENICI [continuing]. Sandia, that's different and run under different law, but we're trying to bring them both under the same umbrella. The Bhye-Dole changes Dole, by Dole cleared you up because you're university regents managed. But they left out, for instance, the private sector, even if it's not for profit. Is it fair to say both are suffering from the same disconnect that was spoke of?

Dr. BELL. Well, in the case of Los Alamos and Livermore, the so-called weapons laboratories, why, there are additional carriers.

Dr. COOK-DEEGAN. I would say, in connection with this, I think what we're talking about is only a small part of the picture but I think it's an important part, and that's the intellectual property protection. So I think it's probably the most important thing.

It sounds like one of the things that you're worried about in the long run is transfer of the knowledge abroad, and probably the best way to make sure that economic benefits accrue to people in the United States is to have strong intellectual property protections. It's probably the first line of defense of intellectual transfer.

I would also say that NSF and NIH have had very successful policies in essentially decentralizing their patent processes and DOE is a little bit behind, and I know you're aware of that.

To the extent that that could be fixed, I think it's something that would be an important thing to do.

One other thing that George brought up, though, that I think is equally important is this role of industry and strategic planning. I'm back to that theme again.

And it seems to me there are a couple of things that could be rather concretely incorporated into a set of genome projects. It seems that there are a couple principles that you can think about.

Number one, it seems like there are certain functions that private companies could perform. They can construct instruments, for example, and I know the Livermore group is buying lots of instru-

ments from companies to perform some of the things that they need to do in the routine work.

So that's one principle, is when there are companies that can do something and are already providing services, why don't you pay them to do that. That's relatively efficient.

Number two, when you're trying to decide what to do, I think it's—whatever structure is set in place to decide which government agency is going to be doing which thing and what are the overall priorities for the human genome projects, industry has to have a say in that, they have to.

If there's an advisory committee, there has to be at least a few people who are from biotech companies, pharmaceutical companies, chemical companies, instrumentation companies, who can say this is really interesting and if you spend some money in this direction, we can take it from there.

So that means if there's an advisory committee or a consortium, they need to be part of it.

And the third is, the ideal really is what already happens at the programmatic level. When you're talking about individual scientists in molecular biology, it's very hard to find a prominent molecular biologist who isn't somehow involved with some private company now, and to some degree there's a seamless transition from basic research to applied research in selected areas.

Now, that's not always true in connection with instrumentation and some of the more elaborate things that would be involved in something like this. But that it the ideal, is a seamless transition.

I think that David Kingsbury highlighted the most important thing about that. I think the National Labs have a bit more trouble with that in some cases, and when they do, I think it's largely because of geographical isolation.

I think the way to solve that is to spend some money on moving people around and paying for training, cross-talk, essentially. That's essentially what the Livermore group did when they started out their mapping effort—I don't want to talk for you, Tony, but I mean I think it's a wonderful model.

Dr. CARRANO. You're doing a fine job, Bob. Keep going.

Dr. COOK-DEEGAN. They called up the scientists who were working on yeast and on the nematodes, which were the two organisms in which mapping has gone the furthest, essentially had presentations from those people, talked to a bunch of mathematicians who were involved in setting overall strategy for making this efficient.

They also talked to the company that has the one sequencing machine that's available. Very early on, before the machine was even on the market, in fact, Livermore was talking to the company that makes those machines.

So at the programmatic level, things were moving great but it cost them a lot of money and it took a lot of time to bring all those people to Livermore to give them talks and to send people from Livermore to those places.

I think that's money well spent and it's not an easy thing to budget for, but I think it's something that needs to be built into a program and make sure that there's a line item that says this is for training and for fellowships or whatever, of senior scientists from industry to go to the National Labs, to universities or what-

ever, and make it kind of a common pool so that there's communication.

So it essentially freezes in place what already happens in practice, but it makes it easier to do. It shouldn't take as much energy as it took to do what was done, I think.

Dr. DELISI. If I can just say one thing. It was referred to by both Paul Silverman and George Bell, and I think it hasn't been discussed very explicitly, and that is training.

What the human genome project is about is developing resources that will prepare the nation for the 21st Century biology, and at the same time in developing the resources. I think we need to make sure we have available the talent that's capable of using them.

Now, I think in the strictly biological aspects of this project there's no problem, but a very watched component of it is a massive super computer project. And training in the use of mathematics with computer tools is going to be crucial, and that, as I mentioned before, with respect to drug design, that same development of the private sector is going to be very important.

I can imagine, for example, at Los Alamos, if the University of New Mexico were interested, companies would spring up all around the state, the students would be trained, they come from the state, they would be trained in the state, they would stay in the state and it would be a tremendous boom to the state economy.

So I think training is something which is underlying this but it's not really being explicitly discussed and developed and probably requires a little bit of thought.

Dr. KIRSCHSTEIN. I think Dr. Delisi is absolutely right, but I would like to say that I don't think that training is okay in terms of the biological sciences either.

Formal training in multidisciplinary molecular biology combined with everything else has not been supported very well for the last ten years.

There have been far fewer graduate students supported under the government that there were in the past. The dollars have remained even and the costs have gone up, one of the reasons being that tuition in graduate schools is going up all the time.

Senator DOMENICI. Dr. Oesterling, do you have any comments?

Mr. OESTERLING. Yes, I just want to make a comment on the technology transfer, and based, you know, taking off on the comments that Paul Silverman made.

Actually, we have a situation where technology transfer is a two-way street. In the case of our company, we feel that we have developed what is a valuable resource that we would like to make available for the broader project of mapping and sequencing of the genome, and it's not an easy problem to deal with.

We wrestle with it, we have many meetings in trying to decide what is the way we can do this so we can protect the proprietary interests of the company but we can also make the resource available.

And I think this may happen more and more with some of the research that's going on in our company as well as other companies, and we really want to make this resource available. We want to have it as part of the program.

We think it would be foolish to go back and repeat what we have done and spent the money that we have spent over the past four years to develop it.

Mr. ANDERSON. Could I make a suggestion relative to—

Senator DOMENICI. Please.

Mr. ANDERSON [continuing]. Research in industry. In microelectronics the center of research is now in industry. You don't go to the university to find out what's the latest thing in superconductivity if a breakthrough occurred at IBM.

And increasingly in biology this center of gravity for the advanced research will be in industry. We've got to come to grips with that fact.

So the questions are, how does industry gain access to National Laboratories when that's a good idea, and how does the nation support research in industry.

And the suggestion I would like to make to the latter is this. If there is an across-the-board tax break for research, that's a hemorrhage in the treasury that is rather insupportable.

However, we have here the world's expert on peer review, Dr. Kirschstein, who has chaired many, many discussions. [Laughter.]

Mr. ANDERSON. Now, could we put these two together? Suppose that retrospectively your research is peer review for funding by—for a tax break by the Federal Government, so that the best of research done in industry results in a big tax break. That would have several effects.

First, a rather small amount of money would go a long way, but secondly, industry has a hard time knowing when it has good research, especially basic research. And this would be a gold-plated way of certifying that it was worth supporting.

So if there was a budget for retrospective peer review tax breaks, even though it's small, I think it would have a marvelous leveraging effect on the biotechnology industry.

Now, with respect to the other idea, how do we get into National Laboratories, so far we've talked about how National Laboratories spin things off to industry. And it's been my pleasure to do a fair amount of that.

How do we work the other way around? So I've done a number of experiments, and am still doing them, to see whether it can be done. I've spent money at the Argonne National Laboratory, not too successfully, to get some research done.

I couldn't go and look at the work being done, for example. I interfaced with Herman Post at the Oak Ridge National Laboratory, and that is very, very good. They're willing to help in every possible way. And I'm going to explore the same thing with Los Alamos.

What do we do with inventions and developments that occur in industry where in the national interest it would be best if those patents stayed here.

How are the National Laboratories fully utilizing exploiting those patents?

Now, to date the arrangements haven't been very good, and one of the sticking points is that if you go and spend any time at, say, Argonne, under the arrangements that existed when we made our ar-

rangements, anything we thought of when we were there belonged to them.

The questions are patent rights, intellectual property and follow-on patents. If you work collaboratively with a National Laboratory, do they own all the follow-on patents or not, because many of those are very important. They wouldn't exist unless you had your original patent and unless you began to interface with it.

But I think this is an extraordinarily fruitful area to discuss and one that would result in a wide open, two-way street.

Senator DOMENICI. And your recommendation on the latter, when the street runs into the lab, your recommendation is that we make the law what in that respect?

Mr. ANDERSON. Give maximum ownership to the company that will exploit the work. And if it turns out to be very key, and the company isn't following through too well, there could be arrangements to open up the license.

Dr. KIRSCHSTEIN. It's what the government has in terms of if the university scientists or the university decides not to patent something that the government thinks is worthwhile, the government has march-in right, and that's what you're talking about, I think.

Mr. ANDERSON. That's right. And the DOE traditionally has had unusual march-in rights.

Dr. KIRSCHSTEIN. Whereas we do not.

Mr. ANDERSON. Whereas you do not.

Dr. KIRSCHSTEIN. Incidentally, retrospective peer review is publication and referee journals, as far as I'm concerned.

Mr. ANDERSON. But that's hard to do when——

Dr. KIRSCHSTEIN. Not really.

Mr. ANDERSON [continuing]. An instrument is the policy.

Dr. KIRSCHSTEIN. Well, okay, but——

Mr. OESTERLING. If it's an instrument, but if—I don't have any trouble deciding on the quality of the research that's done in my company.

Dr. KIRSCHSTEIN. No. It's exactly what I said.

Mr. ANDERSON. You're a very small company. Big companies have a bigger problem.

Senator DOMENICI. Well, let me just tell you, in the process of looking at this and look at the nation's expenditure of money for research, while I made a statement 20 minutes ago that we spend more and get less in some objectively measurable way than our competitors in the world, I mean I didn't invent that. That's been delivered to me in a public hearing at least twice, somebody who does that said that is the case.

We are still spending a lot of money on research, but there is a growing problem in that the sliver that is private sector is not growing. As a matter of fact, it is going down.

I have the highest respect for peer review, but let me just tell you what I think right now in terms of the tax code and that. I honestly believe that peer review is in such a state of commotion in the Congress——

Dr. KIRSCHSTEIN. You're right.

Senator DOMENICI [continuing]. I won't use any stronger word than that, that I think if you tried to put it in the tax code it would just literally cause a revolt.

Dr. KIRSCHSTEIN. I agree.

Senator DOMENICI. On the other hand, I haven't failed to consider that you might want to, in a more generic even though not review, give some special new tax break in some areas that we know research ought to be taking place.

We have shrunk the tax credit for research in the new tax code rather than expanding it, and frankly I would almost predict that one of the first things that will break in that tax bill, of course there will be special interests that have a lot more, are making a lot more noise about wanting to change the code, but I think a very large group of people, and I put myself in it, that have been worried about research as a component of the private sector.

I believe one of the first things we will change is to enhance the research tax credit, but I don't think we would ever subject it to some kind of a peer review and I just think it would cause all kind of trouble.

Dr. KIRSCHSTEIN. I agree, yes.

Mr. ANDERSON. Some activity would do it.

Senator DOMENICI. Correct. There are plenty of people in the Congress who want to do away with it right now.

Dr. KIRSCHSTEIN. That's right.

Senator DOMENICI. As a matter of fact, as one of those, Ruth, who leads peer review, I will give you my stock lecture. I really believe that it is most important that you stimulate the peer reviewers to a high level of consideration of what they're doing——

Dr. KIRSCHSTEIN. I agree.

Senator DOMENICI [continuing]. Because they are quite properly accused of becoming very sedentary, very rote.

Dr. KIRSCHSTEIN. I couldn't agree more.

Senator DOMENICI. The last word was nepotinistic, if there is such a word. I just invented it. [Laughter.]

Senator DOMENICI. But when you're in doubt, go where your buddies are.

Dr. KIRSCHSTEIN. Oh, that's right. I agree.

Senator DOMENICI. We're not oblivious to it, we're seeing it.

Dr. KIRSCHSTEIN. I know you are.

Senator DOMENICI. There's a lot of people saying we ought to do something completely different, even if it's regionalize peer review. I don't know whether we will, but I think——

Dr. KIRSCHSTEIN. I have some solutions.

Senator DOMENICI [continuing]. We're a short ways away from modifying peer review in some way. People around here come from places in the country that are very much envied by other places. I mean, you come from the area where people say that's one of the spots in America that gets that, plus the triangle over there around Harvard and MIT and that area, and if you look at the map, they get an excessive quantity of peer reviewed science money and they may be the greatest, but I tell you Congress has to spend the money for everybody and there is a growing feeling, well, when will Alabama get to grow if they can't get some. So they're building them without peer review and putting lots of money in.

I don't know that that's a great idea. I'm just telling you. But I would think that we might seriously consider some areas of scien-

tific research weakness, and if we can't get in a broad tax credit, that at least generically you might be able to define some.

If we get anybody interested in that, we surely will include these kind of areas, there's just no question the ones we're talking about here would be in them, have to be.

Well, let me ask my last question. I think I understand kind of where I'm going. I'm personally going to continue to push very hard with the national government to set some goals in this area and that we find some way to coordinate and at least know what's being coordinated, even if it's some kind of revolving policy making group.

I am confident that we must keep the private sector involved. Now I've learned about the two-way street notion, and I think it's very exciting in terms of patents and the like.

But I'm wondering, on the technical end, is there special area that we ought to consider, or some special way that we ought to consider private sector arrangements right up front in any legislation. I mean, we've talked all around it. We've talked about making sure they're on the policy board and making sure that the feed-in is in the right direction, where they are already out front in some area that we ought to remain involved, but are there any special areas that we already know about that we ought to indicate that we want private sector arrangements made as part of this genome mapping and sequencing?

Dr. KIRSCHSTEIN. The private sector has been able to apply for the research funds in the Federal Government, at least those from NIH, for a long time.

I don't think the private sector takes advantage of that sufficiently, and I would think in this kind of a project it would be worth doing, regular research grants.

In addition, there are, of course, the small business innovation research grants, the SBIR program, in which an awful lot of the genome project is being done right now. There are a number of small companies that are involved in this.

And I would hope that when announcements that are going to come and have come from NIH and DOE, from other places, about this, that people here in this room today will spread the word, and all of us will, too, that the private sector is more than welcome to not only put in research grant applications or contract proposals or whatever, but consortium arrangements with people from the National Labs, people from universities, any setup that one wants.

And I certainly would like to see that happen in a very big way.

Dr. CARRANO. Can I ask a question. In terms of them applying to NIH and government agencies, what happens to the patent rights?

The complaint that I've gotten from the bigger industries, the ones that's worked with us, is that if we go for a government grant, then the question of patent rights becomes an issue.

Dr. KIRSCHSTEIN. Well, it does to some extent but I think that one could work these things out in advance, because our regular scientists do that, and they're working out things with, you know, with universities and small companies. I don't think that's a real issue. I think people use it as an excuse, but I don't think it's a real issue.

Incidentally, at Los Alamos there is about $3 million worth of regular research grants right now coming from NIH.

Senator DOMENICI. Where you all applied to NIH.

Dr. KIRSCHSTEIN. Yes, exactly. And I don't—I put those figures together because we were going to be here in New Mexico. I don't have them for Livermore and Lawrence Berkeley, but I suspect it's equal or more.

Dr. SILVERMAN. Yes, we do about 18 million, I think.

Dr. KIRSCHSTEIN. I just didn't put it together.

Mr. OESTERLING. Speaking for must my own, again my little tiny segment of the private sector, I would say that our company has been extremely successful in the SBIR area. We submitted ten Phase 1 proposals and received eight.

However, I must also tell you that the two that were turned down had to do with genome mapping. They had right—they were smack on genome mapping and——

Dr. KIRSCHSTEIN. Come back with our new announcement. [Laughter.]

Mr. OESTERLING. And we also have——

Dr. KIRSCHSTEIN. With a special study session.

Mr. OESTERLING [continuing]. Have been successful in receiving——

Dr. KIRSCHSTEIN. Phase 2.

Mr. OESTERLING. In Phase 2's, but also in receiving a grant to continue the work that we have started with cystic fibrosis, for which we're very thankful.

I would say that in general there's a definite feeling in the private sector that there is a prejudice against them in the peer review. Whether it's true or not, we have had many grants turned down, and the so-called pink sheets that come back, you know, does not correspond to what we hear back from people who participated in the peer review.

And it's a natural thing to expect because there's really nobody from the private sector, or the private sector I don't believe is well represented, in the peer review process.

We think that that is a detriment to industry submitting proposals for grants from the NIH.

Dr. KIRSCHSTEIN. Ten years ago NIH made a change, because up to that point private sector people were not invited to participate on peer review committees.

The change was made as a result of a recommendation by the committee that Dr. Anderson indicated I served as the chair of, and there have been more and more such individuals serving on peer review bodies, and I would suggest that we're working at it very hard.

Mr. OESTERLING. Good. Well, I'm glad to hear that.

Senator DOMENICI. I wonder if just generally I may ask on this, how wild is the notion of putting private sector, just private sector scientists on the normal peer review process——

Dr. KIRSCHSTEIN. Yeah, that's what I'm saying.

Senator DOMENICI [continuing]. Even if it has nothing to do with private sector applying.

Dr. KIRSCHSTEIN. That's what I'm saying. I'm saying that we're doing that now more and more.

Senator DOMENICI. I don't think we're doing it in NSF.

Do you happen to know?

Dr. DELISI. DOE?

Dr. KIRSCHSTEIN. No, he said NSF. I really don't know about NSF. I can't tell you.

Senator DOMENICI. How about DOE?

Dr. DELISI. Yes, at DOE we don't have panels, we send out mail reviews and, yes, sure, we sent them to whoever's competent.

Senator DOMENICI. So it could be private sector people.

Dr. DELISI. That's right.

Senator DOMENICI. I wonder if NSF does. That's interesting. Why don't you find out. My guess is they don't.

Dr. SILVERMAN. I've served on these NIH ad hoc committees for the small business applications and I know that I have, my colleagues have been from the private sector. I think NIH is moving very well.

Senator DOMENICI. Do you have something?

Dr. COOK-DEEGAN. Yes, Senator. You asked for a couple thing about are there things that are special to the genome project where there might be special arrangements, and I think there are and I just wanted to list a few of them.

One of them, Dr. Bell referred to earlier, and that is centralized data bases, or at least some centralized collection facility for coordinating data bases.

Everybody agrees that that's—there's something special about that. It does have to be centralized, and somebody has to run that. And that's one of the complicated areas—I mean, Ruth can tell you better than I can how difficult it's been to get money for GenBank every year, because they have to pass the hat around to 20 million places before the people pop their money and it's the sort of thing that's hard to support if you're talking out of things that are also high on your priority list. It almost has to be set aside as a special thing.

In the case of genome efforts, I think there are also going to be repositories of materials. That will include cell lines, that is, things that are derived from people, that you want to keep and have access to.

There are going to be clones of DNA, lots and lots and lots of them. There are going to be probes, ways of trying to find out what's in that DNA, lots of repositories.

Again, everybody is going to agree that access to those has to be centralized somehow, although they don't necessarily have to be store in a central location. That's one of the options.

Another function is formatting the stuff that goes into those repositories in the data bases. As of right now, there really aren't any standard formats for mapping, sequencing and cloning efforts.

There are standard formats for the sequence information once it's derived, and those have been set by GenBank in the United States and EMBL in the molecular—the European molecular biology community for the European submissions.

That's an important federal function. And there's also a possibility, I think, of some central services that might turn out to be more efficient, although I think it's still an open question whether sequencing should be done at centralized facilities, where there's one

place that's more efficient than someplace else and therefore, instead of doing it in your own lab you send it off.

I think that's an open question. It's perfectly possible machines would be sufficiently small and cheap that anybody could do it, but I don't know.

Same thing for mapping, same thing for diagnostic tests and doing the sorts of things of trying to find genes in the first place.

There are lots of things where there might be a role for central planning. And the question then becomes how do you set that up, and the consortium arrangement that's in your bill is one way of doing that.

I personally don't know what the best way to structure that sort of organization is. I'm not convinced that I've seen the perfect solution yet.

In your bill, for example, there's a consortium and then there's a kind of an overall policy board, then there's a technical board. So you really have three things and the interdigitations of those things are not too well spelled out.

I don't know how to—I think that's going to take a lot of thought, but I think these are the functions that you need to think about when you're trying to set up that structure.

I think the important thing is to make sure that the people who need to be involved are involved, and that means probably some sort of committee that would involve scientists.

I personally think that scientists and the government people should be on the same committee together, but some people disagree with me on that.

And certainly the industrial folks should be on the same committee. And that needs to be a very public, conspicuous place. And I think this gets back to your giving birth to a mouse.

I think if things are left to the federal agencies in and of themselves, they can be doing a wonderful job, but because of the nature of working under a President and through the executive system, it's hard for them to parade their accomplishments and trumpet them around as much as if they were in the private sector they would do.

So I think that a committee can do that. A consortium is one solution. And in fact, you could make this board the running, the administrative center of whatever goes on.

And I think it is time to experiment. And I think biotechnology is a good place to experiment with novel arrangements for trying to improve tech transfer in the United States.

I think it's especially promising because it's already pretty fertile. As I said before, the universities and companies are already pretty well married. And I think here you just need to maybe give that a higher platform and a little bit more conspicuous presence.

And you need to figure out exactly who you want on that advisory committee and how to appoint it and things like that and how to fund it.

Personally, I think it's simpler if you just have the Federal Government pay for that function of coordination and also pay for these functions that are centralized. And whether you do that through the normal agency budgets or through this consortium ar-

rangement, I don't think it matters, as long as there's some planning process that everybody has bought into.

One of the things that's most conspicuous about the genome project has been the degree of controversy it's generated in the scientific community. And I think the main reason for that is the scientists have felt that they don't have a direct voice in what goes on. That's false.

But the perception has ruled the fact in this case and I think one way to solve that problem again is to put it someplace it's very conspicuous.

Just a final, quick point. The other problem that's faced in trying to structure an international collaboration, there are two issues that come up.

One is there are things that everybody agrees should be international, data bases, DNA sequences. I think everybody thinks that that belongs to mankind, and yet at the other end there are all sorts of instruments and products where every nation that's investing in the research wants to get a return on that.

So I think that one interim solution is to have a planning focus, that is, a commission or a consortium or something like that, and that can serve as the international collaborative arm of the American efforts.

And so if Japan wants to come in and cooperate, then they work through that board. If Europe wants to come in, then they work through that board and perhaps they could sit on it as nonvoting members or something like that.

Senator DOMENICI. Yes, sir.

A VOICE. I have only one comment. I agree there are problems, but the solution has to include another word George Bell used, which was accountability. It's very difficult for a committee in a consortium, without someone to structure it, to be held accountable. So your planning organization committee and all the rest have to be a lot of the virtues you are talking about, but somehow institutionally it has to be set up so that somebody is held accountable when it happens.

Dr. COOK-DEEGAN. I agree with that.

Senator DOMENICI. I think we heard that said earlier in the afternoon, but not in the general wrap-up, as to how you do that. That wouldn't be too hard if the national government basically agreed to the notion of a national policy board. You would have to have an executive, it would seem like, and that executive would have to be responsible from time to time of reporting somewhere as to the accountability of those efforts. It would probably be to Congress, or to the President and the Congress, or something.

Let's try to wrap it up now with just a couple more. Anyone in the audience that has a background in this area want to comment? Obviously, we're more than glad to hear from any of you.

Pete? Dr. Klaw? Anybody else?

A VOICE. Well, Senator, there's the other problem of the antitrust issue when you bring the private sector in the National Laboratories and you get everybody sharing information, and how are you going to handle the antitrust exemptions, or are you going to do it like you've done on the microelectronics? I think that that's

going to show up, and then as you move from R&D into production, how are you going to deal with the antitrust exemption?

Senator DOMENICI. We're not unaware, I think we've intentionally left it out because there are enough models around now, it's a question of what we can get through just a few die-hards in the Congress. And I think the last model we had ready for the semiconductor business and for this, incidentally, had cleared everybody that normally complains about antitrust. [Laughter.]

There are only two or three in the Senate and I think they were not the hang-up in this bill on either of the two major thrusts, so I think that process, if you want to look at what Denise and Paul and a number of others put together, it seemed adequate to us and we thought it could get through.

It was specific enough for the industry that we talked to.

Yes, Pete.

A VOICE. I just wanted to congratulate you, Senator Domenici, for bringing the group together. I think it is important that we get beyond these kinds of discussions and start moving towards establishing the kinds of entities, for example, that you have discussed in your bill, entities that will in fact lay out a plan to start charging various organizations with carrying out that plan, and as Fred said, hold appropriate people accountable in order to deliver, and I think we're moving in that direction.

Senator DOMENICI. I tell you, I want to let anybody else that wants to wrap up here take a couple of minutes. I surely don't want to continue my being the last observation at all, but I think I say this to those who are with the Federal Government, and particularly you, Dr. Delisi, and Ruth, but you are both in kind of different roles in the government, but frankly, an awful lot of good things have occurred by way of coordinating and thinking through in the last 18 to 24 months in this area and a couple of others.

I regret to tell you that I think the perception that somebody mentioned a while ago is a very important and I think the perception is what I expressed a while ago, not only with reference to tech transfer but with reference to really wanting the Federal Government to take the lead in a number of these areas.

I don't know whether we can leave genome mapping and sequencing to the excellent team that is currently collaborating and have a feel out there and a feel in the Congress that it's getting done.

Now, that's maybe unfair, but I think really the perception is that the administration really doesn't want to do any of these things in a very dramatic way and they're not sure, you know, it's sort of like maybe it's our role and maybe it isn't.

That's been around in a number of areas as it applies to DOE, so I personally leave even this seminar without the formal hearings, and I want you all to know, for what it's worth, I'm committed to reducing some of these concepts to legislation and not just to leaving them out there for the executive branch to work out as well as you all are telling me the collaboration is getting.

I just believe we may have a tendency to build monuments, and when we get through with the committee, to mess it up. I understand all that, but I think there's an equal chance here that we would do something constructive in this particular area, and I'm

certain in the superconducting materials that there's something we can do legislatively that will be more helpful than what we've done.

But that's where I am, and I thank all of you for your time and I hope you enjoy your visit up here to Santa Fe and to New Mexico, and I'll leave any closing remarks to any of you that might want to comment.

Dr. KIRSCHSTEIN. Thank you for inviting us, Senator.

VOICES. Yes. Thank you very much.

Senator DOMENICI. Thank you very much.

[Whereupon, at 4:15 p.m. the workshop was concluded.]

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